The bispecific SDF1-GPVI fusion protein preserves myocardial function after transient ischemia in mice.

CXCR4-positive bone marrow cells (BMCs) are critically involved in cardiac repair mechanisms contributing to preserved cardiac function. Stromal cell-derived factor-1 (SDF-1) is the most prominent BMC homing factor known to augment BMC engraftment, which is a limiting step of stem cell-based therapy. After myocardial infarction, SDF-1 expression is rapidly upregulated and promotes myocardial repair. We have established a bifunctional protein consisting of an SDF-1 domain and a glycoprotein VI (GPVI) domain with high binding affinity to the SDF-1 receptor CXCR4 and extracellular matrix proteins that become exposed after tissue injury. SDF1-GPVI triggers chemotaxis of CXCR4-positive cells, preserves cell survival, enhances endothelial differentiation of BMCs in vitro, and reveals proangiogenic effects in ovo. In a mouse model of myocardial infarction, administration of the bifunctional protein leads to enhanced recruitment of BMCs, increases capillary density, reduces infarct size, and preserves cardiac function. These results indicate that administration of SDF1-GPVI may be a promising strategy to treat myocardial infarction to promote myocardial repair and to preserve cardiac function.